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EXAMINER	
MARVICH, MARIA	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/587,101	XIA ET AL.	
	Examiner	Art Unit	
	MARIA B. MARVICH	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-74* is/are pending in the application.

4a) Of the above claim(s) *5-9,20-37 and 40-75* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,10-19,38 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 July 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/1/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-75 are pending in this application.

This application is a 371 of PCT/AU05/00071 which claims benefit to AU 2004900266. A certified copy of PCT/AU05/00071 has been identified associated with the application but not one for AU 2004900266.

Claims 40-75 have been withdrawn as they are directed to "use of" products, which is not a recognized class of inventions under 35 USC 101. Should applicant amend the claims in their response to this office action to put them into compliance with 35 USC 101, they will be treated as newly presented claims and it will be determined at that time if the claims are drawn to the elected invention.

Specification

The disclosure is objected to because of the following informalities: the brief description to figure 3 does not include a description of panel C.

Appropriate correction is required.

Claim Objections

Claims 5-9, 20-37, 44-46, 52, 53, 57-75 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim multiply dependent claims cannot depended from multiply dependent claims. In the case of claim 75, additionally, a claim cannot refer to other multiple claims except in the alternative. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

Claims 1 are objected to because of the following informalities: claim 1 recites a method of administering an agent. However, the claim does not state to what it is administered. It appears as if the agent is administrated to a cell as claim 38 and 39 recited that the agent is added *in vivo* or *in vitro*.

Appropriate correction is required.

Hence claims 1-4, 10-19, 38 and 39 are under examination.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 10-19, 38 and 39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to a method of modulating inflammatory responses by administrating an agent that modulates the functional activity of C-reactive protein wherein down-regulating the activity results in reducing an inflammatory response. The claim is directed to a genus of agents, however, applicants only identify the phospholipids HDL and PLPC.

Hence, this is a "reach-through" claim that requires possession of a compound identified through the claimed methods. The written description requirement under 35 USC 112, first paragraph may be met by sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. Applicant is referred to the Guidelines on Written Description published at FR 66(4) 1099-1111 (January 5, 2001) (also available at www.uspto.gov).

The specification teaches that targeting C-reactive protein is an effective means of reducing inflammatory responses associated with a number of disorders and cell adhesion molecule expression. The specification teaches that the C-reactive protein significantly induced up regulation of adhesion molecules in both protein and mRNA levels. The C-reactive protein-induced expression of these inflammatory adhesion molecules was completely suppressed when the cells were reincubated with a physiological concentration (1 mg/ml apoA-I) of high density lipoproteins (I-IDL) derived from human plasma (native HDL)or reconstituted I-IDL (rHDL) at a very low concentration (0.01 mg/ml apoA-I). In particular, the C-reactive protein-induced upregulation of inflammatory adhesion molecules in HUVEC was 5 completely prevented by HDL via their oxidized phospholipid components. Hence, while applicants claim a genus of agents, applicants teach use of a single species.

While one of skill in the art can readily envision numerable species of agents sequences that are obtained by the instant method, the fact remains that the actual agents with a particular

activity cannot be envisioned any better when the possible choices are narrowed from all possible sequences to all possible agents with a particular function. "Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features." *Ex parte Kubin*, 83 USPQ2d 1410, 1417 (Bd. Pat. App. & Int. 2007) citing *University of Rochester*, 358 F.3d at 927, 69 USPQ2d at 1895. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). Claiming all agents that achieve a result without defining what means will do so is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. In this case, applicants claim a genus of promoter that are not described in the specification.

Given the large size and diversity of fragments that are related by 98% to SEQ ID NO: and the inability to determine which will also have the essential element, it is concluded that the invention must be empirically determined. In an unpredictable art, the disclosure of no species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus.

Claims 1-4, 10-19, 38 and 39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is not based on a single factor but is rather a conclusion reached by weighing many factors (See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter, 1986) and In *re Wands*, 8USPQ2d 1400 (Fed. Cir. 1988); these factors include the following:

The instant claims are drawn to a method of modulating inflammatory responses by administrating an agent that modulates the functional activity of C-reactive protein wherein down-regulating the activity results in reducing an inflammatory response. The method requires administration of an agent to a mammal wherein a number of disorders are treated. The disorders are associated with an inflammatory response as well as to elevated levels of ICAM, VCAM or e-selectin. The scope of the invention is extremely broad in that the agents are any number of agents and the disease any number where in administration means to ensure that targeted cells receive the compound in sufficient amount and for a sufficient time to modulate activity of CRP. Furthermore, the claims are drawn to modulation of CRP levels. When considering this goal, the claims are directed to qualitative and quantitative changes as well as increased and decreased.

The MPEP teaches, "However, claims reading on significant numbers of inoperative embodiments would render claims non-enabled when the specification does not clearly identify

the operative embodiments and undue experimentation is involved in determining those that are operative. Atlas Powder Co. v. E.I. duPont de Nemours & Co., 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984); In re Cook, 439 F.2d 730, 735, 169 USPQ 298, 302 (CCPA 1971). (see MPEP 2164.08(b). In this case, as set forth above, the agents are broadly any number of agents. The targets and disorders as well are numerous. IT is not clear how the method will be designed to target all forms of diseases such that targeted cells receive the compound in sufficient amount and for a sufficient time to modulate activity of CRP. The physiological art is recognized as unpredictable. (MPEP 2164.03.) Case law has established that ' (t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without ~undue experimentation.'" In re Wright 990 F.2d 1557, 1561. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that ' (t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art" The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art. The more that is known in the prior art about the nature of the invention, how to make and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order for it to be enabling. In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving

unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved

This invention is so broad as to read on any number of delivery means. For example, gene delivery has been a persistent problem for gene therapy protocols and the route of delivery itself presents an obstacle to be overcome for the application of the vector therapeutically. Opalinska et al. state on page 511 "[I]t is widely appreciated that the ability of nucleic-acid molecules to modify gene expression in vivo is quite variable, and therefore wanting in terms of reliability. Several issues have been implicated as a root cause of this problem, including molecule delivery to targeted cells and specific compartments within cells and identification of sequence that is accessible to hybridization in the genomic DNA or RNA" and in column 2 of the same page, "Another problem in this field is the limited ability to deliver nucleic acids into cells and have them reach their target. Without this ability, it is clear that even an appropriately targeted sequence is not likely to be efficient. As a general rule, oligonucleotides are taken up primarily through a combination of adsorptive and fluid-phase endocytosis. After internalization, confocal and electron microscopy studies have indicated that the bulk of the oligonucleotide enter the endosome-lysosome .compartment, in which most of the material becomes either trapped or degraded. To date, no single mode of gene transfer has provided a viable option for successful gene therapy protocols. In more advanced studies related to cancer, the art teaches "to bring about a desired therapeutic outcome. Reasonably accurate gene delivery can be achieved by direct inoculation of plasmids or recombinant viruses using a needle position in a tumour deposit." (Russell page 1165, col 2,¶ 4-5). When considering protein therapy, Torchilin and Lukyanov (2003) teach that there are many unresolved problems concerning the delivery of

proteins and peptides such as rapid elimination from the circulation through renal filtration, enzymatic degradation, uptake by the reticuloendothelial system and accumulation in non-targeted organs and tissues and inefficient cell entry (see Box 1, page 260).

The invention recites use of a broad group of therapies to modulate CRP activity. Given the unpredictability of the art, the poorly developed state of the art with regard to predicting the structural/ functional characteristics of compounds, the lack of adequate working examples and the lack of guidance provided by applicants, the skilled artisan would have to have conducted undue, unpredictable experimentation to practice the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-6, 10-14, 17-19, 38 and 39 are rejected under 35 U.S.C. 102(e) as being anticipated by Pepys et al (US 7,390,795; see entire document).

Pepys et al teach methods of administering an agent to a subject with a goal of inhibiting binding of CRP to an autologous or extrinsic ligand, hence modulating the functional activity of CRP (see e.g. abstract and col 9, line 13-67) and reducing inflammatory responses (see e.g. col 2,

line 23-35) as recited in claims 1-3, 38 and 39. Subjects and disorders have a condition characterized by aberrant inflammatory responses such as Crohn's, atherosclerosis, cardiovascular disease, stroke, infection (see e.g. col 3, line 5-67) as recited in claims 4, 10-19 and 39. As evidenced by Libby et al, elevated levels of ICAM, e-selectin and other adhesion molecules are inherently associated with disorders such as atherosclerosis (see e.g. page 1139, col 2, ¶ 4).

Claims 1-6, 10-19, 38 and 39 are rejected under 35 U.S.C. 102(e) as being anticipated by Crooke et al (US 7,425,545; see entire document).

Crooke et al teach methods of administering an agent to a subject with a goal of modulating activity of CRP (see e.g. abstract and col 9, line 13-67) and reducing inflammatory responses (see e.g. col 2, line 23-35) as recited in claims 1-3, 38 and 39. Subjects and disorders have a condition characterized by aberrant inflammatory responses such as diabetes, obesity, atherosclerotic, colonic disease, cardiovascular disease, stroke, infection (see e.g. col 13, line 1-53) as recited in claims 4, 10-19 and 39. Elevated levels of ICAM are inherently associated with disorders (see e.g. example 43).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARIA B. MARVICH whose telephone number is (571)272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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